Impact of Demographic Factors and Systemic Disease on Urinary Stone Risk Parameters Amongst Stone Formers

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This article examines via multivariate analysis the associations between demographic factors and systemic diseases on stone risk parameters in a stone-forming population. A retrospective chart review of adult stone formers who completed 24-hour urine collections from April 2004 through August 2015 was performed. Data was collected on age, sex, race, body mass index (BMI), and diagnoses of diabetes and hypertension. CT imaging and renal/abdominal ultrasonography (within $\pm$6 mo) were reviewed for diagnosis of fatty liver disease. Statistical analysis included Pearson and Spearman correlation analysis, and linear and logistic regression analyses, both univariate and multivariate. Five hundred eighty-nine patients were included. Numerous urinary parameters were significant in association with demographic factors or systemic diseases in a multivariate analysis. Older age was associated with decreased calcium (Ca) excretion ($P = 0.0214$), supersaturation of calcium oxalate (SSCaOx; $P = 0.0262$), supersaturation of calcium phosphate (SSCaP; $P < 0.0001$), and urinary pH ($P = 0.0201$). Men excreted more Ca ($P = 0.0015$) and oxalate (Ox; $P = 0.0010$), had lower urine pH ($P = 0.0269$), and higher supersaturation of uric acid (SSUA; $P < 0.0001$) than women. Blacks had lower urine volume ($P = 0.0023$), less Ca excretion ($P = 0.0142$), less Ox excretion ($P = 0.0074$), and higher SSUA ($P = 0.0049$). Diabetes was associated with more Ox excretion ($P < 0.0001$), lower SSCaP ($P = 0.0068$), and lower urinary pH ($P = 0.0153$). There were positive correlations between BMI and Ca excretion ($P = 0.0386$), BMI and Ox excretion ($P = 0.0177$), and BMI and SSUA ($P = 0.0045$). These results demonstrate that demographic factors and systemic disease are independently associated with numerous risk factors for kidney stones. The mechanisms responsible for these associations and disparities (racial differences) need to be further elucidated.

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KEY WORDS

Kidney stones • Systemic disease • Obesity • Diabetes • Fatty liver

The incidence of urinary stone disease is rising. Emerging data suggest that this may be due, in part, to a parallel rise in the incidence of obesity and obesity-related comorbidities.[1] To explore possible mechanisms underlying this relationship, we examined the association between abnormal urine chemistries in stone formers on 24-hour urine collection and the presence of obesity, diabetes (DM), hypertension (HTN), and fatty liver disease.

The development of kidney stones is impacted by age, gender, and presence of certain systemic diseases. Bidirectional associations have been reported with DM and HTN.[1] Obesity is linked to both systemic diseases, and associations with kidney stone formation have been reported.[1] In a study of three large epidemiologic cohorts, Taylor and associates found that both body mass index (BMI) and waist circumference, two measures of obesity, were positively correlated with the risk of developing an incident kidney stone.[2] In an observational study, Sorensen and colleagues identified a positive correlation between BMI and development of an incident kidney stones.[3]

Several urinary parameters have been linked to kidney stone risk. Some have been reported to be influenced by BMI and the presence of certain systemic diseases. The negative correlation between urinary pH and BMI is well established. Associations between uric acid kidney stone formation and obesity have been reported and low urine pH is the driver.[4] Associations between DM and low urine pH have been demonstrated that may result in a propensity for this cohort to develop uric acid stones.[1] Although both the obese and diabetic cohorts are susceptible to developing uric acid (UA) kidney stones, calcium oxalate (CaOx) remains the predominant stone composition in both. Urinary oxalate excretion is positively correlated with the risk of developing kidney stones. This was reported by Taylor and associates in an analysis of large epidemiologic cohorts.[5] Body weight has been demonstrated to impact urinary oxalate excretion. Lemann and associates reported a highly significant positive correlation between urinary oxalate excretion, body weight, body surface area, and urinary creatinine in healthy non–stone forming adults.[6] Furthermore, obese kidney stone formers have higher urinary oxalate excretion relative to that of non-obese stone formers.[7,8] DM, a condition linked to obesity, has been reported to be associated with increased urinary oxalate excretion.[9] Increased visceral fat has been demonstrated to be associated with the risk of developing both CaOx and UA stones.[10] Fatty liver disease, a condition more prevalent in diabetic and obese cohorts,[11] has also been associated with lower urine pH and kidney stone disease.[12,13]

We undertook a study to define the associations between the demographic factors, systemic conditions, and urinary stone risk parameters to better elucidate their influence on calculus formation. Our hypothesis was that systemic diseases and demographic factors could influence urinary stone risk parameters.

Methods

Institutional review board (IRB) approval was obtained to complete a retrospective chart review of kidney stone patients who completed 24-hour urine collections at the University of Alabama-Birmingham School of Medicine from April 2004 through August 2015. The 24-hour urine collections were performed by the same vendor, Litholink (Itasca, IL). Demographic information captured included age at collection, BMI, sex, and race. Chart review was performed to gather history of a diagnosis of DM and HTN. Imaging reports, including computed tomography (CT) and renal ultrasound (US), performed within 6 months of urine collection were reviewed to identify a diagnosis of fatty liver disease. Urine collections were assessed for accuracy based on criteria based on 24-hour urinary creatinine excretion indexed to body weight as previously described.[14] Inaccurate collections were removed from analysis. For patients with multiple collections, the average of the values was used for the analyses. Stone type was determined by the predominant component (>50%) on stone analysis.

Descriptive statistics, including means and standard deviations for continuous variables, and frequencies and proportions for categorical variables, were calculated for study variables of interest. Correlation analyses of urinary parameters, such as oxalate and calcium, and demographic

TABLE 1

Univariate Analysis of Urinary Parameters by Systemic Disease and Demographic Factor

	Urinary Parameters									
Factor	Vol24	SSCaOx	Ca24	Ox24	Cit24	SSCaP	pH	SSUA	UA24	Na24
Spearman Correlation Coefficient Analysis for Categorical Variables										
Obesity (n = 588)										
Obese	2.0328	6.7315	225.2	43.6694	649.1	1.1790	6.0349	1.0634	0.7256	222.5
Non-obese	1.8898	6.8492	186.8	37.0259	513.5	1.2723	6.1517	0.7697	0.5707	166.5
(*P* value)	(0.0424)	(0.7039)	(0.0005)	(<0.0001)	(0.0002)	(0.2842)	(0.0109)	(<0.0001)	(<0.0001)	(<0.0001)
Fatty Liver (n = 588)										
Yes	2.0336	6.8059	222.6	42.7569	600.2	1.0781	5.9530	1.0623	0.6803	202.1
No	1.9159	6.8189	195.7	38.6700	553.6	1.2754	6.1439	0.08395	0.6158	183.6
(*P* value)	(0.1690)	(0.9714)	(0.0588)	(0.0243)	(0.2749)	(0.0620)	(0.0006)	(0.0083)	(0.0177)	(0.0524)
Hypertension (n = 267)										
Yes	2.0105	6.6699	190.4	40.4484	573.2	1.3663	6.0304	0.9299	0.6130	194.0
No	1.8432	6.2415	183.0	35.7041	565.6	0.9816	6.2592	0.6775	0.5472	153.3
(*P* value)	(0.0962)	(0.3069)	(0.6101)	(0.0259)	(0.8581)	(0.0005)	(0.0007)	(0.0085)	(0.0079)	(<.0001)
Diabetes (n = 275)										
Yes	2.0880	6.3793	189.7	46.2417	576.9	0.8037	5.9141	1.0602	0.6575	204.2
No	1.9024	6.4065	188.6	35.3855	563.3	1.2905	6.2192	0.7160	0.5635	166.3
(*P* value)	(0.0981)	(0.9531)	(0.9429)	(<0.0001)	(0.7723)	(<.0001)	(<.0001)	(0.0034)	(0.0042)	(0.0002)
Sex (n = 589)										
Male	2.0580	6.8262	217.7	43.7165	603.4	1.1655	6.0319	1.0267	0.7008	209.4
Female	1.7958	6.7926	180.1	34.1991	514.5	1.3261	6.2014	0.7016	0.5382	159.6
(*P* value)	(0.0001)	(0.9160)	(0.0002)	(<0.0001)	(0.0066)	(0.0575)	(0.0001)	(<.0001)	(<.0001)	(<.0001)
Race (n = 589)										
White	1.9733	6.8751	205.8	39.9954	573.1	1.2544	6.1131	0.8612	0.6307	187.7
Black	1.6655	6.2585	159.4	35.0476	483.6	1.0863	6.0567	1.0629	0.6090	183.0
(*P* value)	(0.0058)	(0.2350)	(0.0044)	(<0.0001)	(0.0387)	(0.2233)	(0.4398)	(0.1189)	(0.4795)	(0.6640)
Pearson Correlation Coefficient Analysis for Continuous Variables										
BMI (n = 588)										
(*P* value)	(0.0008)	(0.3450)	(0.0001)	(<0.0001)	(<0.0001)	(0.0111)	(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)
Age (n = 589)										
(*P* value)	(0.0004)	(<0.0001)	(0.0100)	(0.0604)	(0.3331)	(<0.0001)	(<0.0001)	(0.0003)	(0.3123)	(0.5634)

and diagnostic variables were performed using Pearson correlation analysis, or Spearman correlation analysis when one of the demographic or diagnostic variables was categorical. For continuous data, comparisons of means of urinary parameters were performed using the two-group *t* test, or analysis of covariance while accounting for covariates (demographic or diagnostic) of interest. Linear regression analyses, univariate and multivariate, were used to examine the relationships between the predictor variables and the urinary parameters. Logistic regression analyses, univariate and multivariate, were used to examine the relationships between diagnostic variables. Separate analyses for stone composition was not undertaken as most stones were CaOx and the low percentage of the other categories would not permit meaningful statistical analysis. Distributions of continuous variables were examined using box plots, stem-and-leaf plots, normal probability plots, and the Kolmogorov-Smirnov test; it was determined that these variables did not deviate greatly from a normal distribution. Statistical tests were two sided and were performed using a significance level of 5% (ie, $\alpha = 0.05$). Statistical analyses were performed using SAS software, version 9.4 (SAS Institute, Inc., Cary, NC).

K24	Mg24	P24	NH424	Cl24	Sul24	UUN24	PCR	Cr24	Cr24Kg	Ca24kg	Ca24Cr24
62.6812 50.4106 (<0.0001)	106.6 91.4986 (0.0002)	1.0950 0.8652 (<0.0001)	36.8348 32.3107 (0.0028)	208.3 157.4 (<0.0001)	41.5194 32.1685 (<0.0001)	11.6971 9.0052 (<0.0001)	0.8660 0.9415 (0.0001)	1841.8 1449.9 (<0.0001)	17.0013 19.3510 (<0.0001)	2.1254 2.5472 (0.0003)	127.5 132.9 (0.4013)
59.9930 53.6230 (0.0087)	102.2 95.8380 (0.2293)	1.0435 0.9267 (0.0018)	36.8469 33.3337 (0.0462)	192.2 172.4 (0.0008)	40.3940 34.4369 (0.0016)	11.2413 9.6999 (0.0001)	0.9220 0.9115 (0.6638)	1769.0 1552.1 (0.0005)	18.4011 18.5007 (0.8146)	2.3860 2.3914 (0.9704)	132.5 130.5 (0.8144)
59.4226 49.6348 (0.0004)	96.8564 89.6441 (0.1946)	0.9237 0.8289 (0.0167)	30.8240 30.2673 (0.7886)	186.7 145.9 (<.0001)	36.5089 28.7604 (<.0001)	10.1683 8.3849 (0.0001)	0.8677 0.8775 (0.7041)	1683.1 1449.8 (0.0003)	18.0568 18.8311 (0.1203)	2.0820 2.4460 (0.0303)	118.5 129.3 (0.2162)
65.5610 51.7959 (<.0001)	100.4 91.9790 (0.2181)	1.0005 0.8505 (0.0032)	31.7589 30.3959 (0.5514)	198.1 157.9 (<.0001)	39.4666 31.0769 (0.0039)	11.2105 8.8137 (<.0001)	0.9104 0.8640 (0.1073)	1706.2 1531.9 (0.0153)	17.7119 18.6302 (0.0964)	2.0047 2.3531 (0.0615)	114.0 127.7 (0.1531)
61.0884 47.2816 (<.0001)	110.4 80.4683 (<.0001)	1.0856 0.7821 (<.0001)	37.0550 30.1993 (<.0001)	196.1 151.5 (<.0001)	41.0229 28.8961 (<.0001)	11.4676 8.71797 (<.0001)	0.9490 0.8689 (<.0001)	1897.0 1220.5 (<.0001)	20.1224 16.4432 (<.0001)	2.3402 2.4515 (0.3334)	116.4 148.9 (<.0001)
55.8464 47.1602 (0.0061)	98.1404 88.0437 (0.1002)	0.9650 0.8265 (0.0045)	34.4253 30.3707 (0.0779)	177.2 168.3 (0.3796)	35.5676 36.1563 (0.7797)	10.0573 9.5526 (0.3422)	0.9219 0.8392 (0.0087)	1589.6 1652.2 (0.3696)	18.5427 17.9933 (0.3211)	2.4533 1.8392 (0.0010)	134.1 102.5 (0.0012)
(<0.0001)	(<0.0001)	(<0.0001)	(0.0004)	(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)	(0.0225)
(<0.0001)	(0.8669)	(0.9842)	(0.0215)	(0.1810)	(0.0033)	(0.0098)	(0.5921)	(0.3617)	(<0.0001)	(<0.0001)	(0.0025)

Results

There were 589 patients included in the study. The average age of patients at collection was 50.5 years (range, 18-87 years). There were more men in the study population: 327 men (55.5%) and 262 women (44.5%). Most patients were white (white 89.6%, black 10.4%). Obese patients accounted for 37.2% of the group and the average BMI was 29.3 kg/m^2 (range, 12.2-62.6 kg/m^2). History of DM and HTN was identified in 26.9% and 53.2% of our population, respectively, which was higher than national rates. Both US and CT imaging were available for review in 18.7% of patients, whereas CT imaging alone was available for 61.2% of patients and US imaging alone was available for 4.1% of patients. Only 16.0% of patients had no imaging modality available for assessment. A diagnosis of fatty liver was made radiologically in 19.7% of patients. Most patients were CaOx stone formers (67.5%), with calcium phosphate (CaP) and UA stones being the second and third most common, 18.1% and 12.2%, respectively.

Univariate analysis of each urinary value with demographic factors and systemic disease states revealed many significant associations. Results of this analysis are summarized in Table 1. Multivariate analyses were subsequently performed using BMI as a

TABLE 2

Multivariate Analysis of Urinary Parameters Including Systemic Diseases and Demographic Factors

	Urinary Parameters									
Factor	Vol24	SSCaOx	Ca24	Ox24	Cit24	SSCaP	pH	SSUA	UA24	Na24
Age (*P* value) (+ older age) (− older age)	+0.1799	−0.0262	−0.0214	+0.1971	+0.1813	−<0.0001	−0.0201	+0.6444	−0.0013	+0.0052
Sex (*P* value) (+ males) (− males)	+0.0694	+0.3811	+0.0015	+0.0010	+0.1221	−0.2183	−0.0269	+<0.0001	+<0.0001	+<0.0001
Race (*P* value) (+ Caucasian) (− Caucasian)	+0.0023	+0.6755	+0.0142	+0.0074	+0.0192	+0.5438	+0.0770	−0.0049	+0.1604	+0.1586
Diabetes (*P* value) (+ Diabetes) (− Diabetes)	+0.7321	−0.4435	+0.4336	+<.0001	+0.8894	−0.0068	−0.0153	+0.0881	+0.3281	+0.1363
Fatty Liver (*P* value) (+ Fatty Liver) (− Fatty Liver)	+0.5952	−0.6917	+0.1717	+0.3750	+0.4168	−0.3969	−0.1808	+0.7157	+0.6019	+0.7923
BMI (*P* value) (+ higher BMI) (− higher BMI)	+0.2146	+0.8969	+0.0386	+0.0177	+0.0127	−0.6053	−0.0670	+0.0045	+<0.0001	+<0.0001
Hypertension (*P* value) (+ Hypertension) (− Hypertension)	+0.6896	+0.7154	+0.6959	+0.5458	+0.2234	+0.3737	−0.3929	+0.6195	+0.3531	+0.0052

+, positive association; −, negative association.

Significance defined as $P < 0.05$.

continuous variable (Table 2) and results are subsequently discussed

Multivariate Analysis

Age. With increasing age, there are statistically significant positive correlations with 24-hour sodium, phosphorus, chloride, and creatinine excretion. There are statistically significant negative correlations with age and pH, supersaturation of CaOx (SSCaOx), supersaturation of CaP (SSCaP), and with age and 24-hour calcium excretion and UA excretion. There are negative correlations with age and creatinine and calcium excretion when indexed to kilogram (kg) body weight.

Sex. There are statistically significant positive correlations with male sex and 24-hour calcium, oxalate, sodium, chloride, creatinine, sulfate, urea nitrogen, UA, potassium, phosphorus, magnesium, and ammonium excretion. Protein catabolic rate, creatinine per kg body weight and supersaturation of UA (SSUA) are also positively correlated with male sex. There are statistically significant negative correlations with male sex and pH, and male sex and calcium indexed to urinary creatinine.

Race. Whites have significantly higher volume and 24-hour calcium, oxalate, citrate, potassium, magnesium, phosphorus, and urea nitrogen excretion than blacks. Calcium excretion indexed to body weight and indexed to creatinine excretion are also significantly higher in whites. Whites also have significantly lower SSUA compared with blacks.

BMI. There is a statistically significant positive correlation between BMI and 24-hour calcium, oxalate, citrate, UA, sodium, potassium, magnesium, phosphorus, ammonium, chloride, sulfate, urea nitrogen, and creatinine excretion. Increasing BMI is also positively correlated with SSUA. There is a statistically significant negative correlation between BMI and

K24	Mg24	P24	NH424	Cl24	Sul24	UUN24	PCR	Cr24	Cr24Kg	Ca24kg	Ca24Cr24
+0.0901	+0.1135	+0.0228	−0.0736	+0.0179	+0.9137	+0.8929	+0.3818	+0.0275	−<0.0001	−0.0056	−0.3157
+<0.0001	+<0.0001	+<0.0001	+0.0092	+<0.0001	+<0.0001	+<0.0001	+0.0005	+<0.0001	+<0.0001	−0.5923	−0.0046
+0.0006	+0.0190	+0.0017	+0.2319	+0.0597	−0.7305	+0.0353	+0.0620	−0.8965	+0.9781	+0.0367	+0.0289
+0.0197	+0.7814	+0.3924	+0.8637	+0.0278	+0.2005	+0.0606	+0.0628	+0.2910	−0.3938	−0.5438	−0.5954
+0.1978	+0.5015	+0.2233	+0.1450	+0.8064	+0.2922	+0.2071	+0.6183	+0.4607	−0.7193	−0.4897	+0.2656
+0.0051	+<0.0001	+<0.0001	+0.0484	+<0.0001	+<0.0001	+<0.0001	−0.0001	+<0.0001	−<0.0001	−0.0025	−0.1454
+0.3567	+0.9512	+0.8441	+0.9327	+0.0037	+0.0595	+0.3240	−0.7790	+0.2823	−0.5922	−0.9649	−0.8806

protein catabolic rate, creatinine per kg body weight, and calcium per kg body weight.

DM. There is a statistically significant positive correlation between DM and 24-hour oxalate, potassium, and chloride excretion. There are statistically significant negative correlations between DM, pH, and SSCaP.

HTN. There are statistically significant positive correlations between HTN and 24-hour sodium and chloride excretion.

Fatty Liver. There are no significant associations between a radiologic diagnosis of fatty liver and the urinary parameters assessed.

CaOx Stone Formers. Amongst CaOx stone formers, a multivariate analysis restricted to fatty liver, BMI, DM, and HTN demonstrated several significant associations. Oxalate ($P < 0.0001$), UA ($P = 0.0304$), potassium ($P = 0.0048$), and chloride ($P = 0.0324$) excretion were positively correlated with DM. HTN demonstrated positive associations with potassium ($P = 0.0500$) and sulfate ($P = 0.0057$) excretions. Fatty liver was associated with increased potassium ($P = 0.0405$) and citrate ($P = 0.0097$) excretions. BMI was positively associated with SSUA ($P = 0.0062$), and excretion of UA ($P = 0.0003$), sodium ($P < 0.0001$), magnesium ($P = 0.0332$), phosphorus ($P = 0.0010$), chloride ($P < 0.0001$), urea nitrogen ($P = 0.0015$), and sulfate ($P = 0.0297$). BMI was positively correlated with creatinine excretion ($P < 0.0001$). BMI was negatively associated with creatinine excretion indexed to body weight ($P = 0.0006$), calcium excretion indexed to body weight ($P = 0.0028$), and protein catabolic rate ($P = 0.0028$).

Discussion

Univariate and multivariate analysis of basic demographic factors and systemic diseases revealed several significant relationships in our study. Various systemic disease processes have been associated

with lifetime risk of kidney stones. These include obesity, HTN, dyslipidemia, gout, and chronic kidney disease.[1] This study is unique as, to our knowledge, this is the most extensive multivariate analysis of urinary stone risk parameters, demographic factors, and systemic diseases associated with the development of kidney stones. In addition, we have identified unique associations between race and these parameters.

We found that age is negatively associated with Ca excretion, SSCaOx, SSCaP, and urine pH. These results are corroborated by previous publications. In a less extensive multivariable analysis, Perinpam and colleagues showed that age was negatively correlated with urinary calcium and oxalate excretion.[15] Otto and associates have demonstrated that older individuals have lower urine pH.[16] Friedlander and colleagues studied stone formers and noted that pH decreased with age.[17] Unique to our analysis was the positive correlation of age with sodium, phosphorus, and chloride excretion. The age effects of calcium excretion may be secondary to differences in handling of intestinal calcium absorption, impaired renal function, and altered vitamin D metabolism[18] with age. Decreasing pH with age may be secondary to impaired renal function.[17] We do not have an explanation for the differences seen in sodium, phosphorus, and chloride excretion.

Our study demonstrated certain sex influences. Stone-forming men have higher calcium, oxalate, sodium, chloride, creatinine, sulfate, urea nitrogen, UA, potassium, phosphorus, magnesium, and ammonium excretion and SSUA. Urine pH was also lower in the male cohort. These relationships have been noted in multiple other studies.[19] The variation between the sexes may be secondary to dietary differences and hormonal influences.[20,21]

We found certain racial differences in urinary stone risk parameters including lower volume, lower calcium excretion, lower oxalate excretion, and higher SSUA amongst blacks. Others have reported that blacks have lower urinary volume.[22] This could be due to increased evaporative fluid loss in this cohort.[23] Lower urinary calcium excretion has previously been reported in blacks.[22,24] This may be due to difference in intestinal and renal calcium handling.[25] The higher SSUA that we found may be due to lower urine volume in this cohort.[26] Our findings of decreased oxalate excretion in black stone formers is unique. Others have not reported this difference.

Our results demonstrated that DM was associated with lower pH, lower SSCaP, and higher oxalate excretion. Others have reported these relationships.[9] The lower SSUA is most likely due to reduced urine pH.

The positive correlation between BMI as a continuous variable and calcium excretion, oxalate excretion, and SSUA is consistent with the reports of others.[15] A negative correlation with this parameter and urine pH approached statistical significance. Previous investigators have reported a negative correlation between BMI and urine pH.[27] The latter relationship is a likely explanation for the positive correlation with SSUA.

HTN has been associated with increased risk for kidney stone formation.[28] Hartman and associates have demonstrated in both univariate and multivariate analyses that HTN impacts various urinary parameters.[29] The univariate analysis findings demonstrated that hypertensive patients had lower urine pH, calcium excretion, SSCaOx, and SSCaP. Multivariate analysis in this same study revealed that there was lower Ca, SSCaOx, and citrate excretion in hypertensive patients.[29] We also found that HTN was associated with lower urine pH. Our results with SSCaP were disparate; hypertensive patients had higher SSCaP.

We did not find associations with presence of fatty liver and urinary parameters. Patel and associates performed a multivariate analysis of the associations with visceral fat and hepatic steatosis and urinary stone risk parameters based on quantified CT measurements. In their multivariate analysis, they found that the increasing percentage of measurable visceral fat area was correlated with lower urine pH.[13] The disparity in results could be due to our not quantifying the amount of fatty deposition.

We were able to perform a multivariate analysis only on those patients with CaOx stones as the numbers of individuals with other stone compositions were limited. Oxalate excretion was positively correlated with DM consistent with our global analysis. BMI was positively associated with SSUA and excretion of UA, sodium, magnesium, phosphorus, chloride, urea nitrogen, and sulfate. These associations are most likely driven by dietary habits, something that we did not capture in this study. BMI was positively correlated with creatinine excretion, a well-known relationship but negatively correlated when creatinine is indexed to kg body weight. This too is expected as those with higher BMI would be anticipated to have an increased percentage of body fat and thus generate relatively lower amounts of creatinine.

Most patients collected one or two 24-hour urine specimens (84%), most prior to the institution of medical therapy. Thus, the

impact of any medical stone preventive therapy on the averaging of multiple collections is thought to be negligible.

Our study has certain limitations, including its retrospective nature. In addition, diet can influence the excretion of urinary analytes and this was not controlled.[30] Finally, our analysis did not include other systemic diseases such as gout, coronary artery disease, and chronic kidney disease, which have been associated with kidney stone formation.

Conclusions

These results demonstrate that both demographic factors and systemic disease are independently associated with numerous risk factors for kidney stones. These results highlight that there are differential risks for individuals to develop kidney stones based on these associations. The mechanisms responsible for these associations and disparities (racial differences) need to be further elucidated. ■

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References

1. Boyd C, Wood K, Whitaker D, Assimos DG. The influence of metabolic syndrome and its components on the development of nephrolithiasis. *Asian J Urol*. 2018;5:215-222.
2. Taylor EN, Stampfer MJ, Curhan GC. Obesity, weight gain, and the risk of kidney stones. *JAMA*. 2005;293:455-462.
3. Sorensen MD, Chi T, Shara NM, et al. Activity, energy intake, obesity, and the risk of incident kidney stones in postmenopausal women: a report from the Women's Health Initiative. *J Am Soc Nephrol*. 2014;25:362-3694.
4. Maalouf NM, Sakhaee K, Parks JH, et al. Association of urinary pH with body weight in nephrolithiasis. *Kidney Int*. 2004;65:1422-1425.
5. Taylor EN, Curhan GC. Oxalate intake and the risk for nephrolithiasis. *J Am Soc Nephrol*. 2007;18:2198-2204.
6. Lemann J Jr, Pleuss JA, Worcester EM, et al. Urinary oxalate excretion increases with body size and decreases with increasing dietary calcium intake among healthy adults. *Kidney Int*. 1996;49:200-208.
7. Eisner BH, Eisenberg ML, Stoller ML. Relationship between body mass index and quantitative 24-hour urine chemistries in patients with nephrolithiasis. *Urology*. 2010;75:1289-1293.
8. Taylor EN, Curhan GC. Body size and 24-hour urine composition. *Am J Kidney Dis*. 2006;48:905-915.
9. Eisner BH, Porten SP, Bechis SK, Stoller ML. Diabetic kidney stone formers excrete more oxalate and have lower urine pH than nondiabetic stone formers. *J Urol*. 2010;183:2244-2248.
10. Kim JH, Doo SW1, Yang WJ, et al. The relationship between urinary stone components and visceral adipose tissue using computed tomography–based fat delineation. *Urology*. 2014;84:27-31.
11. Rinella ME. Nonalcoholic fatty liver disease: a systematic review. *JAMA*. 2015;313:2263-2273.
12. Nam IC. Association of non-alcoholic fatty liver disease with renal stone disease detected on computed tomography. *Eur J Radiol Open*. 2016;3:195-199.
13. Patel ND, Ward RD, Calle J, et al. Computerized tomography-based diagnosis of visceral obesity and hepatic steatosis is associated with low urine pH. *J Urol*. 2017;198:1085-1090.
14. Boyd C, Wood K, Whitaker D, et al. Accuracy in 24-hour urine collection at a tertiary center. *Rev Urol*. 2018;20:119-124.
15. Perinpam M, Ware EB, Smith JA, et al. Effect of demographics on excretion of key urinary factors related to kidney stone risk. *Urology*. 2015;86:690-696.
16. Otto BJ, Bozorgmehri S, Kuo J, et al. Age, body mass index, and gender predict 24-hour urine parameters in recurrent idiopathic calcium oxalate stone formers. *J Endourol*. 2017;31:1335-1341.
17. Friedlander JI, Moreira DM, Hartman C, et al. Age-related changes in 24-hour urine composition must be considered in the medical management of nephrolithiasis. *J Endourol*. 2014;28:871-876.
18. Gallagher JC, Riggs BL, Eisman J, et al. Intestinal calcium absorption and serum vitamin D metabolites in normal subjects and osteoporotic patients: effect of age and dietary calcium. *J Clin Invest*. 1979;64:729-736.
19. Curhan GC, Willett WC, Speizer FE, Stampfer MJ. Twenty-four-hour urine chemistries and the risk of kidney stones among women and men. *Kidney Int*. 2001;59:2290-2298.
20. Yagisawa T, et al. The influence of sex hormones on renal osteopontin expression and urinary constituents in experimental urolithiasis. *J Urol*. 2001;166:1078-1082.
21. Bulusu L, Hodgkinson A, Nordin BE, Peacock M. Urinary excretion of calcium and creatinine in relation to age and body weight in normal subjects and patients with renal calculus. *Clin Sci*. 1970;38:601-612.
22. Taylor EN, Curhan GC. Differences in 24-hour urine composition between black and white women. *J Am Soc Nephrol*. 2007;18:654-659.
23. Wesley NO, Maibach HI. Racial (ethnic) differences in skin properties: the objective data. *Am J Clin Dermatol*. 2003;4:843-860.
24. Whalley NA, Atwell T, Lohse C. Lithogenic risk factors in normal black volunteers, and black and white recurrent stone formers. *BJU Int*. 1999;84:243-248.
25. Peng JB. TRPV5 and TRPV6 in transcellular Ca(2+) transport: regulation, gene duplication, and polymorphisms in African populations. *Adv Exp Med Biol*. 2011;704:239-275.
26. Maloney ME, Springhart WP, Ekeruo WO, et al. Ethnic background has minimal impact on the etiology of nephrolithiasis. *J Urol*. 2005;173:2001-2004.
27. Ekeruo WO, Tan YH, Young MD, et al. Metabolic risk factors and the impact of medical therapy on the management of nephrolithiasis in obese patients. *J Urol*. 2004;172:159-163.
28. Cappuccio FP, Siani A, Barba G, et al. A prospective study of hypertension and the incidence of kidney stones in men. *J Hypertens*. 1999;17:1017-1022.
29. Hartman C, Friedlander JI, Moreira DM, et al. Does hypertension impact 24-hour urine parameters in patients with nephrolithiasis? *Urology*. 2015;85:539-543.
30. Sorensen MD, Kahn AJ, Reiner AP, et al; WHI Working Group. Impact of nutritional factors on incident kidney stone formation: a report from the WHI OS. *J Urol*. 2012;187:1645-1649.